

**CLAIMS**

1. An isolated nucleic acid segment encoding a polypeptide comprising the sequence as shown in SEQ ID NO:2.
- 5 2. The isolated nucleic acid segment of claim 1, wherein the nucleic acid segment comprises the DNA sequence as shown in SEQ ID NO:1.
3. The isolated nucleic acid segment of claim 1, further comprising a promoter operably linked to the region encoding said protein.
- 10 4. The isolated nucleic acid segment of claim 3, wherein said promoter is an inducible promoter, a constitutive promoter or a tissue specific promoter.
5. The isolated nucleic acid segment of claim 4, wherein said tissue specific promoter is a bone specific promoter.
6. The isolated nucleic acid segment of claim 1, wherein said nucleic acid segment is comprised within a viral vector.
- 15 7. The isolated nucleic acid segment of claim 6, wherein said viral vector is selected from the group consisting of an adenoviral vector, a retroviral vector, an adeno-associated viral vector, a vaccinia viral vector, a herpesviral vector and a pox viral vector.
8. The isolated nucleic acid segment of claim 1, wherein said nucleic acid segment is comprised within a non-viral vector.
- 20 9. The isolated nucleic acid segment of claim 8, wherein said non-viral vector is comprised in a lipid carrier.
10. The isolated nucleic acid segment of claim 1, further comprising a region encoding a selectable marker protein.

11. A nucleic acid segment characterized as:

(a) a nucleic acid segment comprising a sequence region that consists of 14 nucleotides that have the same sequence as, or complementary to, at least 14 contiguous nucleotides of SEQ ID NO:1; or

(b) a nucleic acid segment of from 14 to 10,000 nucleotides in length that hybridizes to the nucleic acid segment of SEQ ID NO:1, or the complement thereof, under stringent hybridization conditions.

12. The nucleic acid segment of claim 11, wherein the segment comprises a sequence region of at least 14 contiguous nucleotides from SEQ ID NO:1 or the complement thereof.

13. The nucleic acid segment of claim 11, wherein the segment comprises a sequence region of at least 17 contiguous nucleotides from SEQ ID NO:1 or the complement thereof.

14. The nucleic acid segment of claim 11, wherein the segment comprises a sequence region of at least 20 contiguous nucleotides from SEQ ID NO:1 or the complement thereof.

15. The nucleic acid segment of claim 11, wherein the segment comprises a sequence region of at least 25 contiguous nucleotides from SEQ ID NO:1 or the complement thereof.

16. The nucleic acid segment of claim 11, wherein the segment comprises a sequence region of at least 30 contiguous nucleotides from SEQ ID NO:1 or the complement thereof.

17. The nucleic acid segment of claim 11, wherein the segment is at least 17 nucleotides in length.

18. The nucleic acid segment of claim 11, wherein the segment is at least 20 nucleotides in length.

19. The nucleic acid segment of claim 11, wherein the segment is at least 25 nucleotides in length.

20. The nucleic acid segment of claim 11, wherein the segment is at least 30 nucleotides in length.

21. An isolated polypeptide comprising the sequence as shown in SEQ ID NO:2.
22. The isolated polypeptide of claim 21, wherein the polypeptide is comprised in a pharmaceutically acceptable carrier, diluent or excipient.
23. The isolated polypeptide of claim 22, wherein the pharmaceutically acceptable carrier is a lipid carrier.
24. The isolated polypeptide of claim 23, wherein the lipid carrier is a liposome.
25. The isolated polypeptide of claim 23, further comprising a bone tissue targeting agent.
26. A recombinant host cell comprising a nucleic acid segment encoding a polypeptide comprising the sequence as shown in SEQ ID NO:2.
27. The recombinant host cell of claim 26, further defined as a prokaryotic host cell.
28. The recombinant host cell of claim 27, wherein the prokaryotic host cell is a bacterial host cell.
29. The recombinant host cell of claim 26, further defined as a eukaryotic host cell.
30. The recombinant host cell of claim 29, further defined as a bone cell or bone cell precursor.
31. An antibody that is immunologically reactive with a polypeptide comprising the sequence as shown in SEQ ID NO:2.
32. A polyclonal antisera that is immunologically reactive with a polypeptide comprising the sequence as shown in SEQ ID NO:2.
33. A method of identifying a subject at risk of or suffering from a bone degenerative disease comprising:
- (a) obtaining a bone tissue sample from said subject; and
  - (b) assessing the expression of HA4 in said sample,

wherein a reduced amount of HA4 expression in said sample, as compared to the HA4 expression observed in a healthy subject, indicates that said subject is at risk of or suffers from a bone degenerative disease.

34. The method of claim 33, wherein assessing comprises measuring HA4 mRNA levels or stability.

35. The method of claim 33, wherein assessing comprises measuring HA4 protein levels or stability.

36. A method of treating a bone degenerative disease in a subject comprising increasing the level or activity of HA4 in bone tissues of said subject.

37. The method of claim 36, wherein increasing the level or activity of HA4 comprises administering to said subject a therapeutically effective amount of an expression vector, wherein said expression vector comprises a nucleic acid segment encoding an HA4 polypeptide under the transcriptional control of a promoter.

38. The method of claim 37, wherein the promoter is a constitutive promoter, an inducible promoter or a tissue specific promoter.

39. The method of claim 38, wherein the tissue specific promoter is a bone specific promoter.

40. The method of claim 37, wherein the expression vector comprises a non-viral vector.

41. The method of claim 37, wherein the expression vector comprises a viral vector.

42. The method of claim 37, wherein said expression vector is administered endoscopically, intravenously, intraarterially, intramuscularly, intralesionally, percutaneously, or subcutaneously.

43. The method of claim 37, wherein said expression vector is administered directly to a bone tissue.

44. The method of claim 37, wherein said administration is repeated.

45. The method of claim 36, wherein increasing the level or activity of HA4 comprises administering to said subject a therapeutically effective amount of an HA4 polypeptide.

46. The method of claim 45, wherein the HA4 polypeptide is formulated in a lipid carrier.
47. The method of claim 46, wherein the lipid carrier is liposome.
48. The method of claim 45, wherein the lipid carrier further comprises a bone tissue targeting agent.
- 5 49. The method of claim 45, wherein said HA4 polypeptide is administered endoscopically, intravenously, intraarterially, intramuscularly, intralesionally, percutaneously, or subcutaneously.
50. The method of claim 45, wherein said HA4 polypeptide is administered directly to a bone tissue.
- 10 51. The method of claim 37, wherein said administration is repeated.
52. The method of claim 36, further comprising administering a second agent that induces bone formation.
53. The method of claim 52, wherein said second agent is estrogen, raloxifene, alendronate, salmon calcitonin, a vitamin D analog, fluoride, or a PTH analog.
- 5 54. A non-human transgenic animal, cells of which comprise one allele of the HA4 gene that does not express a functional HA4 product.
55. The non-human transgenic animal of claim 54, wherein said animal is a mouse.
56. A non-human transgenic animal, cells of which comprise an expression cassette comprising an HA4 5'-regulatory region operably linked to a screenable marker gene.
- 0 57. The non-human transgenic animal of claim 56, wherein said animal is a mouse.
58. The non-human transgenic animal of claim 56, wherein the screenable marker gene is luciferase, green fluorescent protein, or  $\beta$ -galactosidase.
- 5 59. A method of expressing an HA4 polypeptide in a cell comprising transferring into said cell an expression construct encoding an HA4 under control of a promoter active in said cell, wherein said expression construct effects the expression the HA4 polypeptide.